

**REMARKS**

The following remarks are offered in response to an interview with the Examiner that was conducted by the undersigned, as the applicant's representative, with Examiner Cheu and Supervisory Examiner Le, on March 27, 2006. The interview related to an Amendment filed on February 6, 2006, which was a response to a final Office Action dated October 5, 2005. The Amendment at issue was not entered prior to the interview.

A listing of proposed claims is presented above: the claims are marked to show changes made relative to the claims previously considered, since the Amendment filed on February 6, 2006, was not entered. The claims substantially correspond to those that were presented and not entered; however, in response to comments made during the interview, the claims have been further amended, relative to those last entered by the Office, as follows:

1. Claim 1 was amended as further explained below to address the Examiner's comments about the size limitation in claim 1. Claim 1 now incorporates a size limitation taken from page 20, line 15, in place of the previous size limitation that appears to be of concern only for definiteness reasons, and not for distinguishing any specific references.

2. Claim 117 was canceled in light of the size limitation amendment to claim 1.

3. New claims 120 and 121 are proposed: these claims separate the subject matter of claim 1, which recites two alternative limitations for the claimed microdevice, into two separate claims, each containing only one of the alternative limitations. Either one of these limitations is believed to distinguish the claimed device from all cited art. Claim 120 now covers a microdevice of claim 1 that meets only the first of these alternative limitations, and claim 121 covers a microdevice that meets only the second of these two limitations. Accordingly, if a reference provides basis to reject only one of the alternative limitations in claim 1, one of these two claims would still be patentable, and the claims depending from claim 1 could properly depend from it.

These above listing of claims reflects these amendments.

**The Telephonic Interview**

The applicant appreciates the courtesy of a telephonic interview with Examiner Cheu and Supervisory Examiner Le, conducted on March 27, 2006, and the quick delivery of a summary of the interview to the applicant's representative by Examiner Cheu. From the interview, the applicant's representative understands that the Examiner is willing to reconsider refusal of entry of the amendment previously submitted, and may withdraw the anticipation rejections based on Kaye after further consideration of the content of the Kaye reference. Further comments regarding obviousness rejections based on Kaye were invited by the Examiner, and are provided herein. The Examiner agreed to consider the following comments in deciding if the amendment would place the claims in condition for allowance, subject to any additional searching the Examiner finds necessary. The applicant greatly appreciates the Examiner's time and assistance with this matter.

**Supplemental Remarks**

The following remarks are intended to supplement, not to replace those provided in the last response; thus they do not repeat the description of support for all of the proposed amendments or rebut each specific point in the previous Office Action as the previous response did. Instead, they highlight the differences between the claimed invention and the Kaye reference, which are believed to justify withdrawal of the anticipation rejection as discussed during the interview. They also demonstrate that Kaye should not support an obviousness rejection, either alone or in combination with the references cited in the last Office Action.

As the Examiner's summary indicates, the interview was focused on the Kaye reference cited in the last Office Action. The Kaye reference, GB 2 306 484, is entitled "Solid support particle marked with a machine-readable code for use in Combinatorial Chemistry Techniques." Kaye relates to "A solid support particle (preferably of silicon, silicon dioxide or a metal), adapted for use in Combinatorial Chemistry Techniques, [that] is marked with a machine-readable code." (From the Abstract of Kaye). The device in Kaye is apparently designed to permit a user to track a particular particle while it is used for the synthesis of molecules using, as the title says, combinatorial chemistry techniques. Tracking is enabled by marking each particle with a machine

readable code. The surface of the Kaye particles is a material which can serve as a chemical support on which combinatorial synthesis can be performed.

The presently claimed invention relates to a microdevice that includes an optically readable code, permitting each particle to be identified; the claimed microdevice also includes a 'binding partner capable of binding to a moiety to be manipulated.' Thus the microdevice of the invention includes a feature that can be used to bind and carry a separate moiety.

In response to the rejections based on Kaye in the last Office Action, claim 1 was amended to recite two alternative limitations that are believed to clearly distinguish Kaye. The proposed claims require a device to meet at least one of two alternative limitations, each of which was taken from dependent claims. Those limitations are discussed individually to demonstrate that Kaye does not anticipate or render obvious either of the two alternative limitations.

#### **The 'Magnetic Material' claim limitation**

First, the claimed device can "comprise[] a magnetic material". This is taken from dependent claims 13 and 28-29, which claimed a device comprising a magnetic material, or an element that facilitates manipulation of the microdevice (claim 28), which element can be a magnetic material among others (claim 29). A magnetic material is one of the means disclosed in the application to manipulate the microdevices of the present invention with a physical force. Incorporation of a magnetic material enables the user of the device to move a particle around, such as on a chip, using magnetic forces, which can greatly facilitate automation of certain uses of the device.

#### **A. Anticipation**

Kaye does not appear to disclose any magnetic materials for its device, as was discussed during the interview. Kaye describes preferred materials for constructing its device at page 11, lines 11-21. It describes silicon, silicon dioxide, and metals as suitable materials, because it is known that code marks can be applied to these materials by micromachining. Preferred materials named

are silicon and silicon dioxide; and the only metals mentioned as such structural components are gold and aluminum. None of these is a magnetic material.

A specific passage in Kaye was cited against the claims that included a magnetic material as a claim limitation. However, as was discussed in the interview, that passage in Kaye (pg. 15, lines 12-17) describes “individual materials which can be altered by application of an external non-chemical stimulus, for example electromagnetic radiation.” This is understood by the applicant’s representative to refer to a method for writing a “machine-readable code” onto the Kaye particle. It clearly refers to “electromagnetic radiation”, e.g. light or radio waves rather than to a magnetic material, and the next sentence in Kaye says, “By virtue of the changes imbued in them by the particular stimulus, these materials can, by suitable readout of the residual deposits, reveal the process sequences that those particles/subparticles have experienced.” This seems to indicate that the electromagnetic radiation ‘stimulus’ causes a change in the particle, and the ‘residual deposits’ are understood to be merely imprints or modifications of the polymer / silicate structure rather than any physical deposits of material. (An electromagnetic radiation treatment would not be able to physically deposit any material, but it could either change material already present or remove material, as by laser engraving.) Thus Kaye seems to say that the applied stimulus, which can be electromagnetic radiation, makes the particles readable; but it does not seem to provide means or motivation to add magnetic material to the particle. Accordingly, Kaye is not believed to anticipate this claim limitation, since it does not disclose any magnetic material incorporated into its device.

## **B. Obviousness**

Kaye also does not appear to suggest the desirability of adding a magnetic material, especially since none of the disclosed components is magnetic. Kaye does not suggest adding any element to facilitate manipulation of its particles, which is the purpose served by the magnetic material in the claimed invention. Indeed, since the purpose of the Kaye particle is to serve as a substrate for combinatorial chemistry (combi chem) synthesis reactions, the inertness of the materials is a paramount design consideration.

Kaye provides that the coded material and the combichem substrate material of its particle may be one phase or they may be separate phases (page 5, lines 1-7), and that the coded material may be encapsulated within the combichem substrate (page 5, lines 8-11) or may be attached to it (page 5, lines 13-20) if they are separate phases. However, the preferred materials for the coded portion (silicon oxides) and the particular, apparently less preferred metals named for it (gold, aluminum), are all relatively inert chemically. This suggests that an inert material is desirable, perhaps to keep the coded portion material from affecting chemical reactions in which the particles are used for combinatorial synthesis. The nature of that material could affect the combichem reactions using these particles if the material is exposed either by the design selected for the particle, or by flaws in manufacture of the particles or damage to the particles during use.

As one of ordinary skill would appreciate, use of a relatively inert coded material decreases the likelihood that the materials used to make the particles would affect the usefulness of the particles for their intended combichem applications. Kaye, pg. 8, last line, suggests the particle should be made “of a chemical composition which is not affected by the rigours of library synthesis...” Kaye suggests that inert materials are important for its particles, so it implicitly teaches away from using commonly recognized magnetic materials such as iron alloys in its particles. A less inert material could corrode if exposed to the “rigours” of combichem usage or it could act as a catalyst, as some transition metals are known to do. Kaye thus provides no motivation to include a magnetic material; implicitly teaches away from the use of common magnetic materials in favor of using chemically inert components; and provides no guidance that would permit one of ordinary skill to select a suitable magnetic material. Accordingly, Kaye should not support an obviousness rejection of the ‘magnetic material’ claim limitation.

In the Office Action, Kaye was combined with Zhou, WO 00/054882 to reject claims 12 and 14; this was based on the conclusion that using materials disclosed in Zhou in a device according to Kaye would be an obvious variation of Kaye. However, such substitution is only prima facie obvious for art-recognized equivalents, or where the required properties of a particular element are clearly spelled out and one can simply select a suitable material according to the specified properties. Zhou focuses on using its device, which is an “array chip”, “for directed

manipulation, synthesis and release of biomolecules” (Zhou abstract), rather than for combichem applications, so the Zhou device would not have the same stringent materials limitations that apply to the Kaye particles. Kaye’s particles are expected to encounter reaction conditions known to damage biomolecules; those conditions could degrade a less inert material, and the combichem reactions could be affected by a metal that would either corrode or have catalytic activity under the particular combichem reaction conditions used. Thus materials suitable for use in Zhou’s devices, even if they included magnetic materials, are not necessarily suitable for use in the Kaye particles. And Zhou does not demonstrate that the materials it discloses are art-recognized equivalents that can predictably substitute for the materials used in Kaye for making a particle designed as a combinatorial chemistry substrate. Accordingly, Zhou does not provide motivation to include a magnetic material in the Kaye particle, and Kaye teaches away from using the commonly recognized magnetic materials, so the combination of Kaye with Zhou should not render the ‘magnetic material’ claim limitation obvious.

### **The ‘Binding Partner’ claim limitation**

Second, the binding partner of the claimed device can “comprise[] a cell, a cellular organelle, a virus, or an antibody.” This is a modified list of such binding partners taken from dependent claim 26: the list was modified by replacing the broader term ‘molecule’ from that list with the more specific term ‘antibody’ taken from the specification (see pg. 22, ll. 25-31 and pg. 45, ll. 5-7). This list of specific binding partners clearly distinguishes the device in Kaye, which is designed for stepwise synthesis of molecules using combinatorial chemistry techniques, and would clearly not be suitable for making any of these binding partners.

#### **A. Anticipation**

Kaye relates to a combinatorial chemistry support; accordingly, it discloses a solid support that can include any number of inert polymeric materials and silicates. However, it also says that the material “is of a chemical composition which is not affected by the rigours of library synthesis...” (pg. 8, last line) That is clearly an important aspect of the Kaye device, which is designed for solid phase synthesis applications. And Kaye itself notes that oligonucleotides and

peptides “are generally sensitive molecules which are unlikely to withstand some of the harsh reaction conditions...necessary for the preparation of a broad variety of ligands.” (Pg. 3, ll. 22-24, discussing reasons that oligonucleotides and peptides are not suitable markers for combinatorial chemistry supports.) Accordingly, the Kaye particle could not comprise any of the binding partners recited in the amended version of claim 1 and remain useful for the purpose for which the Kaye device was designed.

The passage in Kaye that was cited against claim 26 in the Office Action is page 2, lines 1-5. That passage is in the background section of the Kaye patent, which describes “exposing the library to a biological or chemical system of interest” to identify compounds that may inhibit or stimulate an enzyme or receptor. Thus it is not disclosing a use of the Kaye particles per se. Instead, this passage describes a use for a library that could theoretically be made with a device like that described in Kaye; it does *not* describe a version of or a use of the Kaye device itself. Such a library might be synthesized with the Kaye device, but it is not a feature of the device. Nor is such a library disclosed by Kaye, which does not appear to describe any library syntheses. Even if a library were made with the Kaye device, though, and tested with a biological target, that would only create a possibility for binding of a biomolecule to the particle from Kaye. Thus Kaye does not anticipate claim 1 even by inherency, since inherent anticipation requires that the missing feature must *necessarily* be present—the mere possibility that a Kaye particle could in theory, *after* modification of the particle to make it display a combinatorial chemistry reaction product, bind to a biological molecule, does not support an inherent anticipation rejection. See MPEP 2112. (IV).

Kaye does not disclose a particle that comprises any of the biological binding partners required by the binding partner limitation of claim 1 as amended, nor does it suggest, describe or enable the synthesis of such binding partners on its particle, so Kaye does not anticipate claim 1. The possibility that the Kaye device could be used to make a library, which could be screened for binding to various biological targets, and could in theory provide a biological target bound to the particle by its interaction with a combinatorial chemistry product on the particle, is simply too remote and speculative to provide an inherent anticipation of the claimed device. Accordingly, Kaye does not anticipate the ‘binding partner’ limitation of claim 1 as amended.

**B. Obviousness**

Furthermore, Kaye teaches away from the use of the 'binding partners' named in amended claim 1 on its particles, because they are not suitable for use on a particle for combinatorial chemistry reaction conditions. As mentioned above, Kaye discloses that peptides and oligonucleotides would not be suitable features for a combinatorial chemistry support because they would limit the reaction conditions too much. Each of the binding partners recited in claim 1 would comprise at least one such substance. Therefore, one of ordinary skill would not be inclined to use such binding partners with the Kaye device. Accordingly, Kaye should not form a basis for any obviousness rejection of the binding partner limitation of claim 1, since Kaye teaches away from combinations that would add any of the biological entities of claim 1 to its device. Finally, in theory, Kaye's device could be used to screen biological entities if it were first used to construct a combinatorial library, and the screening could form a device bound to a biological entity such as one of those recited in claim 1. This possible 'inherent' formation of such a combination cannot support an obviousness rejection, though, since inherency requires that the combination would necessarily result from the teachings of the reference, and Kaye does not teach any particle with a compound or library attached, or any screens or specific biological targets. Accordingly, the 'binding partner' limitation is neither anticipated nor obvious in view of Kaye.

Certain claims were rejected over Kaye in view of Cattell (US 6,180,351) in the previous Office Action, also. Cattell, however, was cited for its use of certain fluorescent labels. Accordingly, it does not appear to relate to either the 'magnetic material' or the 'binding partner' limitations added to claim 1. Accordingly, it is not believed to be relevant to the anticipation or obviousness of the claims as amended.

**The 'Size' claim limitation**

During the interview, the Examiner also raised a concern that a size limitation of the claimed microdevice in claim 1, which recited a microdevice dimensioned "to about several thousand microns", could be interpreted to include relatively large structures. In the above claim listing, claim 1 is amended to include size limits for the claimed microdevice that are more precise;



this limitation is supported at page 20, lines 14-15: this line refers to an irregular shape, but clearly limits the size to about 1 to about 500 microns. As amended, the size limitation is precise enough to eliminate any indefiniteness concerns and is supported by the specification.


**Conclusion**

In view of the above remarks, the claims as amended herein are believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 471842000500. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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